REMARKS

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action dated July 25, 2007 (hereinafter, "Office Action"). This Office Action was issued subsequent to the Notice of Panel Decision from Pre-Appeal Brief Review mailed May 18, 2007. In the Decision, the rejection under 35 U.S.C. § 103 was withdrawn, and prosecution was reopened.

The Specification is amended herein to delete a hyperlink from the text.

Claims 1, 2, 7-11, 17-19, 47 and 48 are pending. Claims 49-57 are added herein to complete the record, and read upon the invention elected for examination. Support for these new claims can be found throughout the application as filed, for example:

- Claims 49-50 and 57 drawn to polyclonal, monoclonal, humanized or chimeric antibodies: page 4, lines 7-20;
- Claims 51-52 drawn to administering following a coronary artery occlusion: page 11, lines 9-11;
- Claims 53-54 drawn to administering following a myocardial infarction: page 11, lines 9-11; and
- Claim 57 drawn to an antibody that specifically binds to EMAP II of SEQ ID NO: 1: page 13, lines 7-21.

Dependent Claim 56 mirrors pending dependent 47, but depends from new Claim 57. No new matter is added by these new claims, and their entry and examination are respectfully requested.

I. Objection to the Specification

The Specification was objected to as containing an embedded hyperlink and/or other form of browser-executable code. Applicant has deleted the hyperlink that was found on page 8 from the Specification. Therefore it is respectfully requested that this objection be withdrawn.

II. Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1-4, 6-14, and 16-19 stand rejected under 35 U.S.C. § 112, first paragraph, enablement. Specifically, the Office Action states on page 10: "in view of the breadth of the claimed invention, the limited guidance in the specification as filed, and furthermore the lack of clarity in regards to the structure of biologically active EMAP II (as of the filing date of the instant application) targeted in the methods which read on treating any subject, human or otherwise, Applicants have not taught the skilled artisan how to practice the full scope of the claimed invention without undue experimentation." Applicant respectfully disagrees.

The test for enablement is whether one skilled in the art could reproduce the claimed invention without undue experimentation. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). The key word is "undue," not "experimentation," and "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804, 807 (CCPA 1982)). In *Wands*, claims to antibodies that required a screening procedure to isolate the desired hybridoma cells from enormous numbers of other cells present in the reaction mixture were held to not require experimentation that was "undue." *Id.*, 8 USPQ2d at 1406. The amount of effort required to make the antibodies was "not excessive." *Id.*, 8 USPQ2d at 1407.

A. The full range of claimed antibodies are enabled.

Applicant claims antibodies that specifically bind to EMAP II of SEQ ID: 4. As noted in a previous Office Action, mailed November 6, 2001, antibodies to EMAP II were known in the art (page 5). The previous Office Action referred to IDS reference 1 as an example, which is U.S. Patent No. 5,641,867 to Stern et al., and which is also incorporated by reference in the instant application at page 4, lines 17-20. Furthermore, the claimed range of variations on these antibodies are well within the skill of the art. See, e.g., U.S. Patent No. 5,622,700 to Jardieu et al., also incorporated by reference in the specification at page 4, lines 17-20.

As further evidence to support that antibodies to EMAP II were known in the art at the time of filing, the Murray et al. article (cited by the Office Action on pages 5-6) states:

"The preparation and characterization of polyclonal antibodies against recombinant human EMAP-II has been described in detail elsewhere." (page 2046, middle of second column). Murray et al. also notes a study by Schluessener et al. using monoclonal antibodies raised against a portion of EMAP II (page 2046, top of second column). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); see also MPEP § 2164.01.

Furthermore, there is no evidence presented that variation of the type of immunoglobulin or animal of origin of the administered antibodies would necessitate undue experimentation of the pending claims. Thus, there is no reason to doubt that the full range of antibodies as claimed is available to the skilled artisan without undue experimentation.

B. The claims recite treating a human subject with antibodies that specifically bind to a particular human EMAP II amino acid sequence (SEQ ID: 4) and are directed to cardiac muscle tissue.

The Office Action states on page 5: "Applicant's claim to methods comprising the use of antibodies targeting EMAP II appears to be incomplete, and premature since the actual structure of biologically active EMAP II was unknown as of the filing date of the instant application." The Office Action then quotes from Murray et al. and alleges that little is known of the mechanism of EMAP II processing by cells, and that the relationship between the mature form of EMAP II and the putative precursor is not clear. In reply, Applicant notes that there is no evidence that undue experimentation would be required to practice the invention as claimed without having detailed knowledge of the *in vivo* processing of EMAP II.

The Office Action on page 6 refers to Schwarz et al., which discusses *in vivo* distribution of EMAP II, and parenthetically notes an area for further investigation in its concluding paragraphs (page L374). Applicant respectfully submits that this vague statement found in Schwarz et al. is inadequate evidence that undue experimentation would be required to practice the invention as claimed.

On page 7 of the Office Action, Thompson et al. is quoted at page 162 as suggesting that the biologically active form of EMAP II is not consistent in all mammals, and that different forms of the protein may control or regulate different activities in specific tissue

types. In response, Applicant notes that the claims are directed to cardiac muscle tissue. Further, Thompson et al. goes on to state: "Nonetheless, high levels of EMAP II are expressed throughout the 6-week period following myocardial infarction." (page 162, bottom of first column). This statement supports the distribution of EMAP II in cardiac muscle tissue upon myocardial insult or disease.

Stryer et al. is cited by the Office Action on page 8 to say that "a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformation of the protein," to support the assertion that the overall structure of the biologically active form of EMAP II appears to be potentially variable from species to species and from tissue type to tissue type. Again, Applicant notes that the claims recite human treatment with regard to cardiac muscle tissue with antibodies that specifically bind to a particular human EMAP II amino acid sequence (SEQ ID: 4).

C. The working example provided in the specification is reasonably correlated to human treatment.

The Office Action states on page 9 that the specification does not teach how to extrapolate data obtained from *in vitro* or *in vivo* observations as well as clinical experience with EMAP II specific antibodies to the development of effective methods of any immunotherapeutic method broadly encompassed by the claimed invention. However, the *in vivo* animal study disclosed in Example 1 of the present specification is reasonably correlated to the *in vivo* treatment of human subjects, and clinical data is not required:

> Usefulness in patent law, and in particular in the context of pharmaceutical inventions, ***necessarily includes the expectation of further research and development.*** The stage at which an invention in this field becomes useful is ***well before it is ready to be administered to humans***. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential new cures in many crucial areas. . . .

In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995) (emphasis added).

Applicant respectfully submits that one skilled in the art would find the working example in the specification using mice as correlative with respect to other mammalian subjects. Mice are art-recognized models for other mammalian subjects, including humans.

This creates a presumption that studies with mice are correlative with other subjects. "In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate" (M.P.E.P. § 2164.02, "Correlation: *In Vitro/In Vivo*").

D. Conclusion: Claims 1-4, 6-14, and 16-19 are enabled.

In light of the above discussion, there is no reason to doubt that enablement is satisfied for the claimed invention upon weighing the *Wands* factors (see M.P.E.P. § 2164.04). Therefore, Applicant respectfully requests that the rejection of Claims 1-4, 6-14, and 16-19 under 35 U.S.C. § 112, first paragraph, enablement, be withdrawn.

III. Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-4, 6-14, and 16-19 stand rejected under 35 U.S.C. § 112, first paragraph, written description. Specifically, the Office Action states on page 10:

> With the exception of the specific antibody that binds specifically to human EMAP II peptide CDAFPGEPDKELNP for purifying recombinant EMAP II, in the specification as filed, there is insufficient written description about the binding specificity of any and all antibodies that bind to EMAP II of SEQ ID NO: 4 for the facilitation of vascular growth in cardiac muscle of a human subject afflicted with myocardial ischemia, atherosclerosis, myocardial disease, cardiomyopathy or cardiac hypertrophy using any antibody that binds to SEQ ID NO: 4.

On page 10 the Office Action further concludes that Applicant was not in possession of the full scope of possible polyclonal or monoclonal antibodies, antibody fragments, humanized or chimeric antibodies isolated from any suitable source, such as chicken, goat, rabbit, horse, etc., wherein said antibody specifically binds to EMAP II of SEQ ID NO: 4. Applicant respectfully disagrees.

As noted above, antibodies to EMAP II were known in the art at the time of filing (see Office Action of November 6, 2001, page 5), and so were the claimed antibody variations (see, e.g., U.S. Patent No. 5,622,700 to Jardieu et al., incorporated by reference in the specification at page 4, lines 17-20).

Further, in the previous Office Action of May 2, 2006, page 3, it states in support of an obviousness rejection: "Stern et al. discloses antibodies which specifically bind to EMAP

II polypeptide as set forth in SEQ ID NO: 4." As noted above, Stern et al. (U.S. Patent No. 5,641,867) is incorporated by reference in this application. Therefore, these antibodies are adequately described in the specification as filed.

Applicant further notes that the state of the art in this field was highly developed at the time of filing, as reflected by (among other things) the numerous issued United States patents on the therapeutic use of antibodies and the broad commercial availability of techniques for "humanizing" antibodies for therapeutic purposes. Techniques for "humanizing" antibodies were widely available at the time the application was filed, and persons skilled in the art would readily know how to "humanize" antibodies for use in the instant invention through routine product development procedures. Applicant further notes that in view of the skill in the art, claims directed to humanized antibodies merely serve to complete the record.

Accordingly, Applicant respectfully requests that the rejection of Claims 1-4, 6-14, and 16-19 under 35 U.S.C. § 112, first paragraph, written description, be withdrawn.

IV. New Claims 49-57 are Enabled and Adequately Described

New Claims 49-57 are enabled and adequately described for at least the reasons stated above with respect to Claims 1-4, 6-14, and 16-19.

In addition, a previous Office Action, mailed November 16, 2005, noted that monoclonal antibodies targeting EMAP II (Claims 49-50 and 57) were enabled (see pages 7-8) and adequately described (see page 4).

Also, the present Office Action on page 4 noted that the specification discloses antibodies such as monoclonal and polyclonal antibodies generated from the peptide consisting of the amino acid sequence DAFPGEPDKELNP (which corresponds to SEQ ID NO: 1) wherein the antibody binds specifically to human endothelial-monocyte activating polypeptide (EMAP) II (independent Claim 55 and its dependent Claims 56-57).

Finally, Applicant has added claims directed to administering the antibodies following coronary artery occlusion (Claims 51-52) and following myocardial infarction (Claims 53-54) in response to the remark in the present Office Action (on page 4) that the pending claims do not include the recitation of administration of anti-EMAP II antibody subsequent to ligation of the left anterior descending artery.

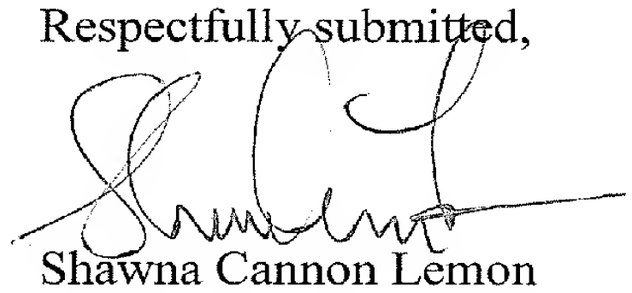
Therefore, new Claims 49-57 are enabled and adequately described, and Applicant respectfully requests that they be entered, examined and allowed to issue in the present application.

V. Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

No fees are believed due. In the event that additional extension is necessary to allow consideration of this paper, such an extension is hereby petitioned for under 37 C.F.R. § 1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully submitted,



Shawna Cannon Lemon
Registration No. 53,888

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428
Raleigh, North Carolina 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401

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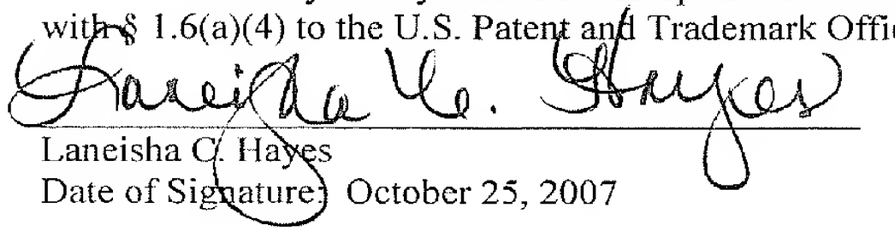

Laneisha C. Hayes
Date of Signature: October 25, 2007